AMENDMENT

Kindly amend the application, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows.

IN THE SPECIFICATION:

Kindly amend the specification without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows:

Page 1, line 1, paragraph previously added in response to Restriction Requirement of September 23, 2002 (paper no. 12) under heading "Related Applications":

This application is a continuation-in-part of US 09/246,191, filed December 30, 1998, which claims priority from US provisional application 60/070,488, filed 5 January 1998. Reference is also made to: the concurrently-filed US application of Andersen et al., Serial No. 09/804,980; US application Serial No. 09/289,388 filed 12 April 1999, which is a continuation of US application Serial No. 08/465,640 filed 5 June 1995, now US Patent No. 5,955,077, issued September 21, 1999, which is a continuation-in-part of US 08/123,182 filed 20 September 1993, now abandoned, and a continuation-in-part of PCT/DK94/00270 ~~PCT/DK94/00273~~, filed July 1, 1994, published as WO95/01441, and claiming priority from Danish application 0798/93, filed July 2, 1993;US application Serial No. 09/050,739 filed 30 March 1998, which is claims priority from US provisional application Serial No. 60/044,624 filed 18 April 1997; Andersen et al., application Serial No.09/791,171, filed 20 February 2001, as a divisional of U.S. application Serial No. 09/050,739; and commonly-owned U.S. Patent No. 6,120,776.

C1

Page 2, lines 26-32:

Animal tuberculosis is caused by *Mycobacterium bovis*, which is closely related to *M. tuberculosis* and within the tuberculosis complex. *M. bovis* is an important pathogen that can infect a range of hosts, including cattle and humans. Tuberculosis in cattle is a major cause of economic loss and represents a significant cause of zoonotic infection. A number of strategies have been employed against bovine TB, but the approach has generally been based on

C2

government-~~organised~~ organized ~~programmes~~ programs by which animals deemed positive to defined screening test are slaughtered.

Page 7, lines 23-31:

Each polypeptide may thus be ~~characterised~~ characterized by comprising specific amino acid sequences and be encoded by specific nucleic acid sequences. It will be understood that such sequences include analogues and variants produced by recombinant or synthetic methods wherein such polypeptide sequences have been modified by substitution, insertion, addition or deletion of one or more amino acid residues in the recombinant polypeptide and still be immunogenic in any of the biological assays described herein. Substitutions are preferably ''conservative''. These are defined according to the following table. Amino acids in the same block in the second column and preferably in the same line in the third column may be substituted for each other. The amino acids in the third column are indicated in one-letter code.

C3

Page 12, lines 8-22:

In order to identify relevant T-cell epitopes which are ~~recognised~~ recognized during an immune response, it is possible to use a "brute force" method: Since T-cell epitopes are linear, deletion mutants of the polypeptide will, if constructed systematically, reveal what regions of the polypeptide are essential in immune recognition, e.g. by subjecting these deletion mutants e.g. to the IFN-γ assay described herein. Another method utilises overlapping oligopeptides for the detection of MHC class II epitopes, preferably synthetic, having a length of e.g. 20 amino acid residues derived from the polypeptide. These peptides can be tested in biological assays (e.g. the IFN-γ assay as described herein) and some of these will give a positive response (and thereby be immunogenic) as evidence for the presence of a T cell epitope in the peptide. For the detection of MHC class I epitopes it is possible to predict peptides that will bind (Stryhn et al 1996) and hereafter produce these peptides synthetically and test them in relevant biological assays e.g. the IFN-γ assay as described herein. The peptides preferably having a length of e.g. 8 to 11 amino acid residues derived from the polypeptide. B-cell epitopes can be determined by ~~analysing~~ analyzing the B cell recognition to overlapping peptides covering the polypeptide of interest as e.g. described in Harboe et al, 1998.

C4

Page 13, lines 6-11:

C5

Immunogenic portions of polypeptides may be ~~recognised~~ recognized by a broad part (high frequency) or by a minor part (low frequency) of the genetically heterogenic human population. In addition some immunogenic portions induce high immunological responses (dominant), whereas others induce lower, but still significant, responses (subdominant). High frequency><low frequency can be related to the immunogenic portion binding to widely distributed MHC molecules (HLA type) or even by multiple MHC molecules (Kilgus et al. 1991, Sinigaglia et al 1988).

Page 19, lines 28-31:

C6

The invention also pertains to a method for ~~immunising~~ immunizing an animal, including a human being, against TB caused by virulent mycobacteria, comprising administering to the animal the polypeptide of the invention, or a vaccine composition of the invention as described above, or a living vaccine described above.

Page 19, line 33 to page 20, line 3:

C7

The invention also pertains to a method for producing an immunologic composition according to the invention, the method comprising preparing, ~~synthesising~~ synthesizing or isolating a polypeptide according to the invention, and solubilizing or dispersing the polypeptide in a medium for a vaccine, and optionally adding other *M. tuberculosis* antigens and/or a carrier, vehicle and/or adjuvant substance.